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PRINCIPAL INVESTIGATOR: Henry Thompson, Ph.D.

CONTRACTING ORGANIZATION: Colorado State University
Fort Collins, Colorado 80523-2002

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13. ABSTRACT (Maximum 200 Words) The primary objective of this project is to determine whether selenium supplementation affects candidate markers of breast cancer risk in a cohort of women at elevated risk for breast cancer. The intermediate biomarkers to be studied are: indicators of oxidative damage to cellular macromolecules such as DNA and lipid, indicators of IGF metabolic status, and cellular indicators of breast cancer risk. We propose a randomized, placebo-controlled, double-blind chemoprevention trial with 150 participants (75 subjects per arm) using a placebo tablet or a tablet containing 200 µg high-selenium brewer's yeast per day, given for a duration of one year. The form and dose of selenium that will be used has been reported to reduce cancer incidence and mortality in lung, prostate, and colon. Blood and urine will be collected at baseline, and after 6 and 12 months of intervention. The feasibility of obtaining breast epithelial cells via nipple aspiration at baseline and the end of the intervention is being assessed. Plasma selenium and glutathione peroxidase activity will be evaluated in addition to pill counts and self report as markers of compliance.				
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Introduction

The primary objective of this project is to determine whether selenium supplementation affects candidate markers for breast cancer risk in a cohort of women at elevated risk for breast cancer. The intermediate biomarkers being studied are: indicators of oxidative damage to cellular macromolecules such as DNA and lipid, indicators of IGF metabolic status, and cellular indicators of breast cancer risk.

Body of Report

Approved Statement of Work

We are conducting a randomized, placebo-controlled, double-blind chemoprevention trial with 150 participants (75 subjects per arm) using a placebo tablet or a tablet containing 200 µg high-selenium brewer's yeast per day, given for a duration of one year. Blood and urine are being collected at baseline, and after 6 and 12 months of intervention. Efforts are being made to obtain breast epithelial and/or breast fluid via nipple aspiration using a modified breast pump. This procedure is performed at baseline and the end of the intervention. Randomization will be in 15 blocks of 10 subjects each.

1. Year 01

- a. Final development of project materials including Web-based randomization program, data entry screens, data quality assurance procedures, project databases.
- b. Obtain all supplements.
- c. Initiate recruitment and enter 3 blocks of 10 subjects.
- d. Schedule follow-up visits.
- e. Institute monthly patient follow-up.
- f. Ongoing collection and analyses of biological samples.
- g. Enter results into databases.
- h. Submit progress report.

2. Years 02-03

- a. Enter remaining subjects into the study and continue follow up, sample collection and analyses. Goal is 8 blocks of 10 in year 02 and 4 blocks of 10 in year 03.
- b. Submit progress reports.

3. Year 04

- a. Complete follow up and the collection and analysis of all samples.
- b. Evaluate all data.
- c. Summarize findings for publication and submit final report.

Acronym for Study We refer to this project as the **ENRICH** study.

Progress on Year 03 Objectives

- a. **Enter remaining subjects into the study and continue follow up, sample collection (and analyses. Goal is 8 blocks of 10 in year 02 and 4 blocks of 10 in year 03.**

As of August 24, 2004, 112 women have been enrolled in the project. The average Gail Score of the women enrolled is 3.0 (5-year risk) which is consistent with this cohort being at increased risk for breast cancer. This represents the three-quarter mark in achieving our enrollment goal. Recruitment continues to be the most challenging aspect of this project since women at risk generally have developed very regimented lifestyle habits that they are hesitant to change (discussed below). Hence, our approach to achieve enrollment goals has been to discuss the project with as many

women at increased risk that we can identify. To facilitate this activity, an additional clinical coordinator was brought on staff for a period of 6 months in order to bolster our recruitment effort.

Of the women enrolled, 36 have withdrawn. This is about 7% higher than we had projected. More than half who have dropped out did so after randomization but prior to attending their baseline clinical visit. The most common reasons for withdrawal have been stated to be inconvenience or not wanting to follow various aspects of the clinical protocol, e.g. limiting alcohol consumption or discontinuing the use of dietary supplements other than the one provided. The most common reason for declining to participate is discontinuing the use of dietary supplements other than the one provided. Relative to withdrawal from the study, we anticipate that the current rate will typify the remainder of the accrual process and is unavoidable. The issues of convenience, alcohol consumption, and supplement use have either already been addressed or are defined by the study protocol.

Compliance Pill count data indicate that compliance is in excess of 97%. Plasma selenium analysis by group is consistent with high compliance; there is very little overlap in the two distributions. Moreover, the maximum plasma selenium levels being measured also indicate that participants are well within safe and acceptable levels of intake.

Nipple Aspirate Fluid In the year 01 Annual Report, we noted the difficulty of obtaining nipple aspirate fluid from many participants and when it was obtained the problem of the adequacy of the cellular content for cytological analyses. Our current rate of success in obtaining NAF is in excess of 50% and our overall project success rate is 30%. Cell content remains low and for this reason, we continue to work on the use of proteomic analysis of either NAF or serum as a biomarker for cancer risk that would replace cytological analysis of NAF in evaluating the effect(s) of selenium on disease risk.

Routine biostatistical audit The most recent audit conducted by the project biostatistician indicates that the accuracy of data entry into the database is above 95%. There were no errors detected in the random sample audited.

b. **Submit progress report.** This document

Key Research Accomplishments Enrollment is proceeding and we have passed the three-quarter point in accrual. Because of the double-blind study design, no biological data is currently available.

Reportable Outcomes (cumulative)

- Supporting intervention materials were developed and tested (when appropriate).
- The project database was completed
- Participants are being enrolled

Conclusions Work is progressing as planned with continuing attention focused on completing accrual. Alternative approaches to cell-based risk assessment using NAF continue to be evaluated.

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